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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/696,814

10/30/2003

David Goldberg

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EXAMINER

GAKH, YELENA G

ART UNIT

PAPER NUMBER

1743

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/696,814

Applicant(s)

GOLDBERG, DAVID

Examiner

Yelena G. Gakh, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 October 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/30/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Election of claims 1-11 and 21 filed on 01/18/07 is acknowledged. The restriction is not considered to be traversed, if the Applicants do not provide any arguments regarding restriction requirements and cancel all non-elected claims. Claims 1-11 and 21 are pending in the application.

Drawings

2. Schematic algorithm of the method steps depicted on Figures 3-6 cannot be considered an illustration to the claimed invention, since it is not quite apparent, as to what the monosaccharide set table is, how peak identification is performed, and what is the results summary (Figure 3). It is further unclear, as to what are monosaccharide combination ranges, what type of rule set should be developed, etc. The examiner considers the method steps depicted on Figures 3-6 more appropriate for description in the text, with more illustrative examples for performing method, such as representing monosaccharide set table or assigning cartoons to the peaks in a real mass spectrum necessary for better understanding of the invention.

Thus, the Applicants are required to furnish additional drawing under 37 CFR 1.81(c). No new matter may be introduced in the required drawing. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d).

The required drawings must illustrate at least one row of the monosaccharide set table comprising 5 HexNAc and 4 Hexoses with a particular mass (page 6, subparagraph [0025] of the specification); the drawings must illustrate assigning glycan cartoons to mass spectral signals.

Specification

3. In Incorporation by Reference the numbers used for US. Patent Applications are in fact numbers for patent application publications. Correct number for applications should be provided, or the names for the applications should be changed to US Patent Application Publications.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to as not containing “a written description of the invention ... in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains” to make or use the invention in its best mode. First, it is not apparent, as to how the references fully incorporated into the instant application are related to the instant invention, since they refer to totally different chemical entities, i.e. peptides and proteins, which are analyzed by different algorithms. Further, it is not apparent from the specification, which mass spectra of glycans are analyzed - mass spectra of unfragmented ions or mass spectra of glycan fragments, which would require different algorithms, since calculating masses of all possible fragments of a particular glycan is different from calculating a mass of the unfragmented glycan. Also, cartoons would be different for fragmented and unfragmented glycans. Regarding the term “cartoons” itself - while such terms as “carbohydrates” and “proteins” do not require description provided in the specification, since these are well established names of classes of chemical compounds, the term “cartoon” is not so well established in mass spectrometry of glycans. There are several ways of pictorial description of glycans. The term “cartoon” should be clearly defined in the specification in order to avoid ambiguity of its meaning.

Further, on page 5, subparagraph [0025] the phrase “each row of the monosaccharide set table represents a set of glycan isomers, i.e. the different isomers that are comprised of that particular set of monosaccharides” is totally unclear. Which “that particular set of monosaccharides” is meant in the phrase? Where is the “set of monosaccharides” depicted in the Table? The examiner did not find any set of monosaccharides in the drawings. Is the set of monosaccharides a cartoon? The description is not clear.

It is unclear, how the set of glycans is formed in the Table. It is not apparent, as to what is the cartoon dictionary. Is it a dictionary of all possible glycans represented by cartoons?

Which rules are indicated in [0029]? Are these the rules for generating larger sets? Are these also other rules?

The specification raises many questions regarding the clarity and definiteness of the inventive method. The examiner wonders, if the Applicants own article published in Proteomics

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in 2005 (“Automated annotation of matrix-assisted laser desorption/ionization N-glycan spectra”) is a more detailed and clear description of the same disclosure?

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-11 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 21 recite, “receiving not less than one glycan spectrum from a mass spectrometer”. It is not apparent, as to how it would be possible to obtain less than one spectrum from a mass spectrometer? On the other hand, it is not apparent, as to what would be obtaining two, three or more mass spectra from a mass spectrometer? Would these be different mass spectra of the same glycan? Would it be tandem mass spectrometry? The expression is not clear. It is further not apparent, as to what is meant by the description of the spectrum as including “peaks having a measured mass”. Any mass spectrum will contain peaks with a measured mass. The expression is not clear.

Claims 1 and 21 further are unclear and indefinite regarding the recited method steps. It is totally unapparent, as to how “assigning glycan identifications to said peak” occurs. It appears that “assigning glycan identifications to said peaks” is one of the top priority tasks for glycane analysis, which is solved in various ways by different scientific groups described in a number of references. In this light it is not clear, as to how it would be possible for any person of ordinary skill in the art to go from the step of receiving “not less than one glycan spectrum” to the step of “assigning glycan identification to said peaks” without any intermediate well described steps? The claim obviously omits essential steps, which are necessary for performing the method recited in the claim. It appears that at least the recitation of claim 2 should be a part of the method recited in claims 1 and 21.

Claim 2 is not clear. What does it mean, “a plurality of isomers corresponding to glycans”? Which plurality is meant here? Glycan comprises specific monosaccharides. Mass

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spectra do not provide differentiation between monosaccharide isomers. Which plurality is meant here? That fits a theoretical mass of a glycan? Moreover, if the “glycan identifications” (what is this?) are already assigned by the method recited in claim 1, it is not clear, as to why the constructing of a monosaccharide set table recited in claim 2 is necessary at all?

In claim 3 it is not clear, a set of which monosaccharides each row represents. Is this a combination of possible monosaccharide isomers, which fit the total mass of the glycan? What are the “combination ranges”? How a rule set is developed, which specify monosaccharide combination limitations? It is not apparent, why a “glycan isotope frequency” appeared at the end of the claim, as it was not mentioned anywhere else, and how it is taken into account when performing the previous steps of the method? The claim is not written in a clear and definite language.

In claim 4 it is not clear, how the received glycan spectrum is calibrated, and how the isotopes of separate monosaccharides can be matched to the peaks within the glycan spectrum, if the glycan was not fragmented to monosaccharides? Also, the term “isotope of monosaccharide” does not seem to be technically correct.

Claim 5 is unapparent. What is “setting said calibration explicitly”? The examiner does not understand the recitation of the claim.

In claim 6, according to the definition given in the specification, “isotope” means one of two or more atoms having the same atomic number but differing in atomic weight and mass number. It does not fit the recitation of claim 6, which renders claim 6 unclear and indefinite.

It is not apparent, if claim 7 recites an error range.

In claim 8 it appears that it should be “mass *for* a selected peak”, rather than “mass *of* a selected peak”, since the peak does not have a mass. It is not apparent, if the isotope envelopes are computed for naturally occurring isotopes or for isotope labeled molecules. It is not clear, how measuring proximity of the measured mass for a selected peak to the theoretical mass of the glycan is related to the step of computing isotope envelopes. Also, the limitation “said isotope envelopes” does not have an antecedent basis, since neither claim 7, nor claim 4 recites “an isotope envelope”.

Claim 9 is not clear. How is it possible to perform a spectrum combination by combining information from a plurality of spectra? Which information is meant in the claim? Which plurality of spectra is recited in the claim? The claim is not clear and definite.

Claim 10 is totally unapparent. The examiner does not understand the recitation of the claim and therefore is not capable of its senseful interpretation.

In claim 11 it is not clear, how the cartoons are related to the rows in the glycan set table?

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. **Claims 1-5, 9-11 and 21** are rejected under 35 U.S.C. 102(a) as being anticipated by Lohmann et al. (Proteomics, July 2003).

Lohmann teaches a method for automated interpretation of mass spectra of complex carbohydrates, comprising receiving mass spectra of glycans, constructing a monosaccharide set table with “a plurality of isomers corresponding to glycans” (Figure 4), assigning “glycan identification to said peaks” and reporting said peak assignment (Figure 6). The method further comprises constructing a glycan/monosaccharide set chart with a set of monosaccharides, applying combination ranges for said monosaccharides, developing a set rule and eliminating monosaccharides, which do not fit the set rule (see Figures 2-3 and paragraph 2.3). “The monoisotopic or average masses are calculated with a resolution of one mDa. The algorithm works quite efficiently so that all possible fragments of a complex carbohydrate can be calculated within a few milliseconds” (paragraph 2.3, page 2031, right column).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. **Claims 6-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Lohmann in view of Yergey et al. (Anal. Chem., 1983).

Lohmann does not specifically teach calculating isotope envelope and choosing the best isotope envelope for experimental peaks.

Yergey teaches importance of calculation of isotopic distribution in mass spectra of large molecules for correct calculation of mass spectra of large molecules.

It would have been obvious for any person of ordinary skill in the art to modify Lohmann's method by computing isotopic envelope and taking into account isotopic distribution for glycans, because it improves the quality of theoretical prediction of mass spectra, as expressly indicated by Yergey.

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. *Dell et al. (Science, 2001)* teach "glycoprotein structure determination by mass

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spectrometry”; *Cooper et al. (Nucleic Acids Research, 2001)* teach “GlycoSuiteDB: a new curated relational database of glycoprotein glycan structures and their biological sources”. The following non-prior art is closely related to the Applicants’ disclosure: *Lohmann et al. (Nucleic Acids Research, 2004)* teach “GlycoFragment and GlycoSearch MS: web tools to support the interpretations of mass spectra of complex carbohydrates”; *von der Lieth et al. (Briefings in Bioinformatics, 2004)* teach “bioinformatics for glycomics: status, methods, requirements and perspectives”; *Fernández-de-Cossilo et al. (Rapid Comm. Mass Spectrometry, 2004)* teach “automated interpretation of mass spectra of complex mixtures by matching of isotope peak distribution”; *Lütke et al. (Glycobiology Advance Access, 2005)* disclose “GLYCOSCIENCES.de: an internet portal to support glycomics and glycobiology research”; *Goldberg et al. (Proteomics, 2006)* teach “automatic determination of O-glycan structure from fragmentation spectra”.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

3/4/07



YELENA GAKH
PRIMARY EXAMINER